AMENDMENTS TO THE SPECIFICATION

Pursuant to 37 C.F.R. § 1.121(b)(1)(i), Applicants respectfully request that the Examiner replace paragraph [0028] of the published patent application with the following paragraph:

> Figures 21A and 21B show that the cells are resident fibroblasts. Having excluded the possibility that the interstitial cells in poly-D-glutamic acid treated rats are not infiltrating blood cells, the possibility that these cells may be resident fibroblasts was examined. CD73 or 5'-nucleotidase is a surface marker protein specific for the resident fibroblasts in kidney. Using a specific antibody to CD73 surface antigen, it was confirmed that the proliferating interstitial cells in the poly-D-glutamic acid treated rats are in deed resident fibroblasts. (See Figure 21A) The saline treated rat kidneys also show the labeling for resident fibroblasts, which is expected. (See Figure 21A) Positive labeling is identified as brownish color around the nuclei of the cells. (See Figure 21A) Figure 21B shows a negative control for immunohistochemical staining, where primary antibody was omitted from the incubation.

Pursuant to 37 C.F.R. § 1.121(b)(1)(ii), the marked-up version of the replacement paragraph for paragraph [0028] of the published patent application is provided below.

> ~~Figure~~ Figures 21A and 21B ~~shows~~ show that the cells are resident fibroblasts. Having excluded the possibility that the interstitial cells in poly-D-glutamic acid treated rats are not infiltrating blood cells, the possibility that these cells may be resident fibroblasts was

examined. CD73 or 5'-nucleotidase is a surface marker protein specific for the resident fibroblasts in kidney. Using a specific antibody to CD73 surface antigen, it was confirmed that the proliferating interstitial cells in the poly-D-glutamic acid treated rats are in deed resident fibroblasts. (See Figure 21A) The saline treated rat kidneys also show the labeling for resident fibroblasts, which is expected. (See Figure 21A) Positive labeling is identified as brownish color around the nuclei of the cells. (See Figure 21A) Figure 21B shows ~~is~~ a negative control for immunohistochemical staining, where primary antibody was omitted from the incubation.

Pursuant to 37 C.F.R. § 1.121(b)(1)(i), Applicants respectfully request that the Examiner replace paragraph [0029] of the published patent application with the following paragraph:

Figure 22A shows two more profiles of CD73 positive interstitial cells in poly-D-glutamic acid treated rat kidneys. Figure 22B is a kidney section from a Poly-D-Glu treated rat, immunohistochemically labeled for EPO, using an EPO-specific antibody followed by peroxidase-labeled secondary antibody. All proliferating peritubular interstitial cells in Poly-D-Glu treated rats labeled with EPO antibody showing EPO production. (See Figure 22A, second panel)

Pursuant to 37 C.F.R. § 1.121(b)(1)(ii), the marked-up version of the replacement paragraph for paragraph [0029] of the published patent application is provided below.

Figure 22A shows two more profiles of CD73 positive interstitial cells in poly-D-glutamic acid treated rat kidneys. Figure 22B is a kidney section from a Poly-D-Glu

treated rat, immunohistochemically labeled for EPO, using an EPO-specific antibody followed by peroxidase-labeled secondary antibody. All proliferating peritubular interstitial cells in Poly-D-Glu treated rats labeled with EPO antibody showing EPO production. (See Figure 22A, second panel)

Pursuant to 37 C.F.R. § 1.121(b)(1)(i), Applicants respectfully request that the Examiner replace paragraph [0034] of the published patent application with the following paragraph:

Figure 27 shows localization of erythropoietin mRNA in peritubular interstitial cells by in situ hybridization. Formalin-fixed, paraffin-embedded kidneys from saline and Poly-D-Glu-treated rats (250 mg/kg/day for 4 days) were processed for in situ hybridization of EPO mRNA. Messenger RNA in the sections was hybridized using digoxygenin-labeled riboprobes that correspond to EPO gene sequence. The length of these riboprobes was 338 bp. Sites of hybridization were visualized by incubating with peroxidase-labeled antidigoxygenin antibody followed by color reaction with diaminebenzidine (DAB). Figure 27 shows profiles from a saline- treated rat probed with sense riboprobe (Panel A; negative control) or with an anti-sense riboprobe (Panel B). Panel C is from a Poly-D-Glu-treated rat kidney probed with a sense riboprobe (negative control), whereas panel D is from a Poly-D- Glu-treated rat kidney probed with anti-sense riboprobe. The sites of hybridization are seen as lighter color in the peritubular region in panels B and D (arrows).

Pursuant to 37 C.F.R. § 1.121(b)(1)(ii), the marked-up version of the replacement paragraph for paragraph [0034] of the published patent application is provided below.

Figure 27 shows localization of erythropoietin mRNA in peritubular interstitial cells by in situ hybridization. Formalin-fixed, paraffin-embedded kidneys from saline and Poly-D-Glu-treated rats (250 mg/kg/day for 4 days) were processed for in situ hybridization of EPO mRNA. Messenger RNA in the sections was hybridized using digoxygenin-labeled riboprobes that correspond to EPO gene sequence. The length of these riboprobes was 338 bp. Sites of hybridization were visualized by incubating with peroxidase-labeled antidigoxygenin antibody followed by color reaction with diaminebenzidine (DAB). Figure 27 shows profiles from a saline- treated rat probed with sense riboprobe (Panel A; negative control) or with an anti-sense riboprobe (Panel B). Panel C is from a Poly-D-Glu-treated rat kidney probed with a sense riboprobe (negative control), whereas panel D is from a Poly-D- Glu-treated rat kidney probed with anti-sense riboprobe. The sites of hybridization are seen as lighter color in the peritubular region in panels B and D (arrows).